Chapter 4

Oral Microbiology in Periodontal Health and Disease

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Additional information is available at the end of the chapter

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Abstract

Oral microbial community is one of the most complex bacterial florae associated with human body. Up to now, more than 700 different bacterial species have been identified from human oral cavity. Oral bacteria form communities on distinctly different surfaces, such as hard enamel and cementum, as well as on soft epithelial cells. These communities are biofilms, which are characterized by their species composition, their surface or substratum composition, and the conditioning films coating the surfaces on which they form. The composition of the resident oral microflora shows local variations in composition on distinct surfaces (e.g., tongue, cheek, teeth) due to differences in key environmental conditions. Many studies have found that certain microbial flora may be compatible with a state of periodontal health and variations in oral flora is associated with varying degrees of periodontal disease. Information about the composition and the assembly processes of oral microbiota could be used to develop effective strategy and monitoring protocols for periodontal therapy.

Keywords: oral microbiology, periodontal health, periodontal diseases

1. Introduction

Mammals are complex gatherings of mammalian and bacterial cells structured into functional organs, tissues, and cellular communities [1]. Cell-rich bacterial communities are more numerous than human cells in each person with a ratio of 10 bacterial cells to each human cell. In other words, approximately 90% of the cells in and on the human body are microbial cells [2].

The birth of the oral microbiology had been signaled by the fascinating observation of Antony Van Leeuwenhoek (1632–1723), a Dutch dry goods merchant, who observed and described first microorganisms in tartar from his teeth with his primitive microscope. These microorganisms

are now known as some of the abundant bacteria reside in the oral cavity including cocci, spirochetes, and fusiform bacteria [3].

Oral microbial community is one of the most complex bacterial floras associated with human body. Up to now, more than 700 different bacterial species have been identified from human oral cavity. For a long time, the study of oral microbiology has gone through phases of "reductionism" and "holism." In reductionism, the strategy was to understand the whole by examining smaller components. Whereas in holism, microbiologists took the approach of system thinking that helps in understanding of microbial physiology which in turn will have a great impact on oral microbiology by providing invaluable insight into the etiology of dental and periodontal diseases [3].

The human mouth is profoundly colonized by microorganisms, comprising viruses, protozoa, fungi, archaea and bacteria. The normal microbiota of the mouth can act as opportunistic pathogens, and as a consequence of this, many oral diseases such as dental caries and periodontal diseases start to develop [4].

The use of culture-independent methods in determining the composition of the oral microbiome, together with next generation DNA sequencing methods is offering a far deeper analysis than hitherto possible. A combination of phylogenetic, metagenomic, transcriptomic, proteomic and metabolomic methodologies may be required to fully understand oral host-microbiome interactions relevant to health and disease [4].

The purpose of this chapter is to review the properties of the mouth that influence its function as a microbial habitat together with giving a description of the oral microflora associated with periodontal health and disease.

2. The mouth as a microbial habitat

The characteristics of mouth are ecologically different from all other surfaces of the body and control the types of microbes that are able to persist, so that not all of the microorganisms that enter the mouth are able to inhabit in it. The simple presence of the oral microbiota in the mouth inhibits colonization by pathogens, the phenomenon of colonization resistance [5].

The mouth has heterogeneous environments for microbial colonization, diverse habitats exist including, the mucosal surfaces (such as the lips, cheek, palate, and tongue). The properties of these habitats change during the life of an individual.

The growth of distinctive microbial communities is enhanced by the presence of different biological features of these surfaces [6]. Microbial ecology is concerned with the interrelationships between microorganisms and their environments. The most important concept in microbial ecology is the ecosystem which is considered as a complex of organisms in a specified environment associated with nonmicrobial surroundings. Different ecosystems with different assemblage of species and organic and inorganic constituents have been recognized at different sites in the oral cavity.

The site at which a population or a community of microorganisms grows, reproduces or survives is called a habitat, and the function of the microorganism in a habitat is its niche.

The properties of some of the major habitats in the mouth will alter throughout the life of an individual. These changes can be manifested during the first few months of life as the mouth at this time consists only of mucosal surfaces for microbial colonization. Another change will happen when hard nonshedding surfaces appear with the development of the primary dentition, providing a unique surface in the body for microbial colonization. The eruption of teeth also generates another habitat via the development of gingival crevice where the tooth emerges from the gums, and an additional major nutrient source for that site will be obtained from the gingival crevicular fluid (GCF) [6].

In addition, ecological conditions within the mouth will also be affected by the eruption and loss of teeth, the insertion of prostheses such as dentures as well as any dental treatment including scaling, polishing and restorations.

Further fluctuations in the stability of the ecosystem can be induced by external factors including the types of food ingested, periods of antibiotic therapy, and variations in the composition and rate of flow of saliva [6].

The health of the mouth is reliant upon the integrity of the mucosa which acts as a physical barrier by preventing penetration of microorganisms and antigens. In addition to the host defense, factors such as saliva and GCF play an important role in maintaining the integrity of these oral surfaces. For example, saliva contains several anti-bacterial factors, including salivary immunoglobulin A (SIgA) which can reduce or prevent microbial colonization of oral surfaces. Moreover saliva encompasses different types of antimicrobial peptides, including histidine-rich polypeptides (histatins), and cystatins, which may control the levels of yeasts, and a range of active proteins and glycoproteins (lysozyme, lactoferrin, sialoperoxidase) [7].

On the other hand, GCF contains large numbers of viable neutrophils as well as a minor number of lymphocytes and monocytes. Also, GCF can control the ecology of the site in many ways for example removing weakly adherent microbial cells, introducing additional components of the host defenses, and acting as a novel source of nutrients for the resident microorganisms [6].

3. Development of the resident microflora

The human fetus inhabits a sterile environment and from a microbiological point of view, acquisition of resident microflora of any surface influences by successive transmission of microorganisms to the site of potential colonization. It is noteworthy that the human birth is a turning point to its environment from the one that is free of microbe to the one that is microbes dominated.

Within a very short time of delivery, microbes are detectable on those surfaces of the baby that are exposed to the external environment, that is, the eyes, skin, respiratory tract, genito-urinary system, and oral cavity [8].

What is surprising is that despite the neonate's exposure to such a variety of microbes, only a limited number of species are able to permanently colonize the various body sites available, and each site harbors a microbial community comprised of certain characteristic species, that is, the microbes display "tissue tropism."

The mouth is highly selective for microorganisms even during the first few days of life. Only a few of the species common to the oral cavity of adults, and even less of the large number of bacteria found in the environment, are able to colonize the mouth of the newborn [9].

Pioneer organism is a term that defines the organisms to colonize first in a developing ecosystem. The pioneer organisms are capable to alter their environment and make it suitable for colonization by other species [10].

In the mouth, the predominant pioneer organisms are Streptococci and in particular *Streptococcus salivarius*, *Streptococcus mitis*, and *Streptococcus oralis* [11, 12].

The pioneer species are often replaced by other species after they have altered the habitat, making it suitable for colonization by other species by a process called a microbial succession.

There are two kinds of microbial succession. The first one is the autogenic succession in which, the sequence of species is brought about because the resident populations alter their surroundings in such a manner that they are replaced by species better suited to the modified habitat. The second type of succession is the allogenic succession where one type of community is replaced by another because the habitat is altered by nonmicrobial factors for instance changes in the physical or chemical properties of the region or changes in the host [10].

Gradually, the metabolic activity of the pioneer community changes the environment, in that way providing conditions suitable for colonization by a succession of other populations. Factors contributing to succession include changing the local Eh or pH, modifying or exposing new receptors on surfaces for attachment as well as generating nutrients as end products of metabolism (lactate, succinate, etc.) or as break down products which can be used as primary nutrients by other organisms [13].

The early colonizers organisms consist of mainly aerobic and facultative anaerobic species are able to tolerate the high oxygen concentrations and to battle the various removal mechanisms of the oral cavity such as swallowing, chewing, nose blowing and salivary, nasal and crevicular fluid outflow [14].

In a study of 40 full-term babies, a range of streptococcal species were recovered during the first 3 days of life, and *Streptococcus oralis*, *S. mitis biovar 1*, and *S. salivarius* were the numerically dominant species [15].

The replication of early colonized organisms allows the subsequent adhesion of other bacterial species, which though unable to stick to tooth hard surfaces, are quite capable of attaching themselves to already present microorganisms. This is so-called "secondary colonization." As the number of plaque layers' increases, nutritional and atmospheric gradients are created, the oxygen level decreases and the anaerobes can survive [16, 17].

As the multiplicity of the pioneer oral community increases, several species of Gram-negative Anaerobes start to appear.

In a study of edentulous infants with a mean age of 3 months, *Prevotella melaninogenica* was the most frequently isolated anaerobe, as it was recovered from 76% of infants. Additional commonly isolated bacteria were *Fusobacterium nucleatum*, *Veillonella* spp., and non-pigmented *Prevotella* spp. [18].

When the same infants were followed up longitudinally during the eruption of the primary dentition Gram-negative anaerobic bacteria were isolated more commonly, and a greater diversity of species were recovered from around the gingival margin of the newly erupted teeth. These findings confirm that a change in the environment, such as the eruption of teeth, has a major ecological impact on the resident microflora [19].

4. Dental plaque

Communication is a crucial part in successful organizations. Communication between oral microorganisms is essential for initial colonization and subsequent biofilm formation on the enamel surfaces of teeth and necessitates physical contact between colonizing bacteria and between the bacteria and their host [20].

Retention of bacteria to tooth surface prevents it from being swallowing by saliva. Through retention, these bacteria can form organized, intimate, multispecies communities referred to as dental plaque [21].

Dental plaque is structurally and functionally organized biofilm adheres resolutely to tooth surfaces as well as restorations and prosthetic appliances. It is a multi-species biofilm comprising of hundreds of bacterial species, salivary polymers, and bacterial extracellular products. The microbial species colonize the teeth, hard palate, tongue, carious lesions, oral mucosa, and periodontal pockets [22].

The distribution of the microbial species in these plaque biofilms varies depending on the anatomical locations and environmental factors [23].

Dental plaque is classified into supra-gingival and sub-gingival plaques, and both of them have significant contributions to dental and periodontal diseases [22].

The predominant microorganisms of supragingival plaque are Gram-positive facultative anaerobic bacteria particularly *Actinomyces* species, *Streptococci* and *Capnocytophaga* species. The Gram-negative species including *Veillonella* species, *Prevotella* species as well as *Porphyromonas gingivalis* and *Tannerella forsythia*. Whereas the subgingival plaque comprises the following species, *Streptococci, Prevotella denticola*, *Porphyromonas endodontalis*, and *Porphyromonas gingivalis* [24].

The difference between sub- and supragingival plaque as well as between periodontal disease and health is characterized by less proportions of *Actinomyces* spp. and higher proportions of *Prevotella intermedia*, *Prevotella nigrescens*, *Peptostreptococcus micros* and *Fusobacterium* spp. [25].

4.1. Formation of dental plaque

Dental plaque forms through a well-organized sequence of events, ensuing in a structurally- and functionally organized, species-rich microbial community [26].

The stages of plaque biofilm formation include acquired pellicle formation; reversible adhesion involving weak long-range physicochemical interactions between the cell surface and the pellicle, which can lead to stronger adhesin-receptor mediated attachment; co-adhesion resulting in attachment of secondary colonizers to already attached cells; and formation of mature, sub-gingival plaque biofilms [23].

Once dental plaque is formed, the overall composition of its climax community is varied with many species being identified at individual sites. The composition of microbial species in dental plaque is characterized by a degree of stability or balance among the component species. This stability is termed microbial homeostasis, and it is due to a balance carried out by numerous microbial interactions, including examples of both synergism and antagonism [27].

Essential inter-bacterial relationships have been detected in mature biofilms. Such relationships may affect the entire biofilm in general and to some extent the virulence of certain species. These relations are classified as positive or negative.

The positive relationships are known as symbiosis and are classified into three subclasses: mutualism, synergism, and commensalism. Mutualism is a symbiosis in which the bacterial species have equal benefit from their coexistence (*Porphyromonas gingivalis* and *Treponema denticola*; *Tannerella forsythia* and *Fusobacterium nucleatum*). Synergism is the interbacterial relation when the pathogenic potential of both species is superior to the sum of their individual potentials (*Porphyromonas gingivalis* and *Fusobacterium nucleatum*). Commensalism is a bacterial interaction that favors one of the two species (*Porphyromonas gingivalis* and *Campylobacter rectus*).

On the other hand, negative relationships between bacterial species exist in the form of antagonism (*Streptococcus mutans* and *Aggregatibacter actinomycetemcomitans*; *Streptococcus sanguis* and *Aggregatibacter actinomycetemcomitans*) and competitive relations (*Porphyromonas gingivalis* and Gram-positive *Actinomyces viscosus*, *Actinomyces naeslundii*, *Actinomyces israelii*, *Streptococcus mutans*, *Streptococcus mitis*, *Corynebacterium* spp.) [28].

4.2. Quorum sensing in plaque biofilms

As many as 700 diverse species of bacteria have been isolated from the oral cavity [29]. These bacteria exhibit coordinated group behaviors and are responsible for causing periodontal infections as well as dental caries. Bacteria in biofilms come across much higher local cell densities than free-floating, planktonic cell populations (**Figure 1**) [30]. An apparent consequence of this is the elevated levels of metabolic by-products, secondary metabolites and other secreted or excreted microbial factors that biofilm cells encounter. Of particular interest are intercellular signaling molecules called the "quorum-sensing molecules" [31].

Quorum sensing is a process that allows the bacteria to sense one another and to regulate variety of physiological activities and biofilm formation. It was first described for the luminous

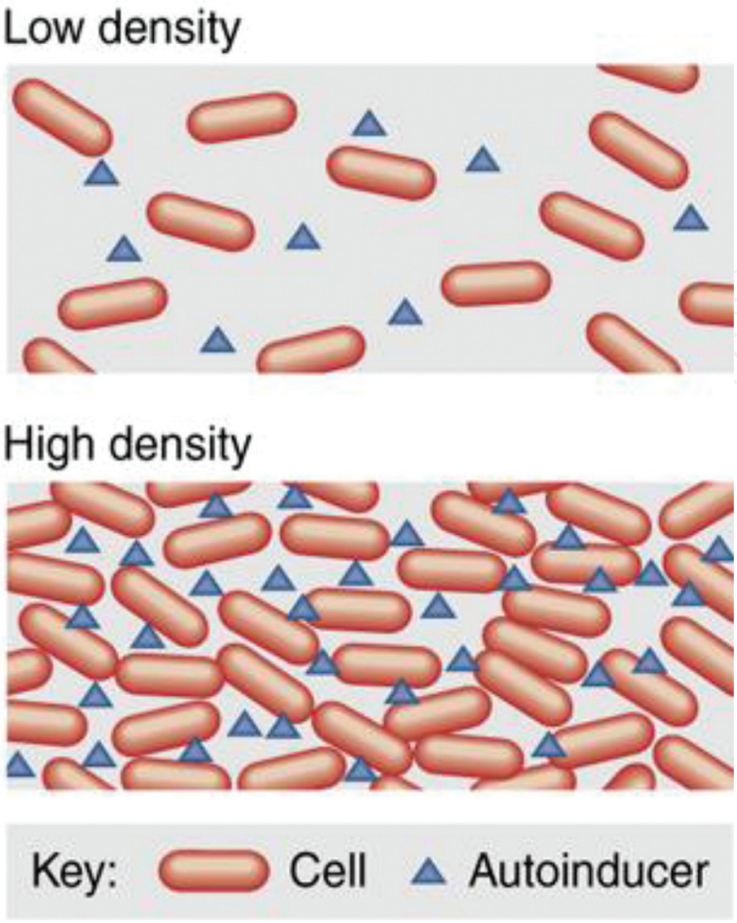

Figure 1. The ability of a cell to produce a signaling molecule (an autoinducer) and sense its extracellular concentration can enable the cell to sense changes in population density [30].

marine bacterium Photo-bacterium fischeri (*Vibrio fischeri*) in 1970 by Kenneth et al. who observed that these bacteria do not luminesce until they reach a high population density. Based on this observation, they postulated that bioluminescence in this organism was possibly controlled by molecular messengers that moved between cells. These messengers were called "autoinducers" [32, 33].

Quorum sensing relies upon the interaction of a small diffusible signal molecule (autoinducers) with a sensor or transcriptional activator to initiate gene expression for coordinated activities. It is extensively used by a variety of Gram-positive and Gram-negative bacterial species to coordinate communal behavior [31].

Quorum sensing systems in bacteria have been generally divided into three classes namely: LuxI/LuxR-type quorum sensing in Gram-negative bacteria, oligopeptide-two component-type quorum sensing in Gram-positive bacteria and luxS-encoded autoinducer 2 (AI-2) quorum sensing in both Gram-negative and Gram-positive bacteria (**Figure 2**) [34].

Quorum sensing permits the bacteria to sense one another and to regulate variety of physiological activities like symbiosis, virulence, motility, antibiotic production, and biofilm formation. Additionally, quorum sensing plays a role in expressing genes for antibiotic resistance

and in promoting the growth of beneficial species to the biofilm and discouraging the growth of competitors [35].

The physiological and clinical aspects of quorum sensing have received considerable attention. It was found that quorum sensing improves the ability of bacteria to increase bacterial defenses against eukaryotic hosts. Furthermore, the gene expression of some bacteria differs in biofilms formed on different dental surfaces and stressful circumstances of adjustment to the surface may persist enhancing intercellular signaling between bacteria [36].

Obviously, many genes and pathways are involved in biofilm formation in different bacteria; moreover, various quorum sensing systems are present in different bacteria. The use of proteomic and genomic techniques should help to elucidate the phenotypes associated with quorum sensing and the mechanisms by which these pathways work in causing periodontal diseases [31].

4.3. The bacterial composition of biofilm in relation to periodontal health

As in other environments, a substantial proportion of the total oral microbiota remains unculturable; therefore, nonculture methods are required to designate the overall species richness of the oral microbiome. Sequence analysis of 16S ribosomal RNA has been the method of choice because of its universal presence in all organisms.

The application of this methodology has led to the description of 11 phyla in the domain Bacteria in the oral microbiome in addition to methanogenic species of the Methanobrevibacter genus from the domain Archaea [37].

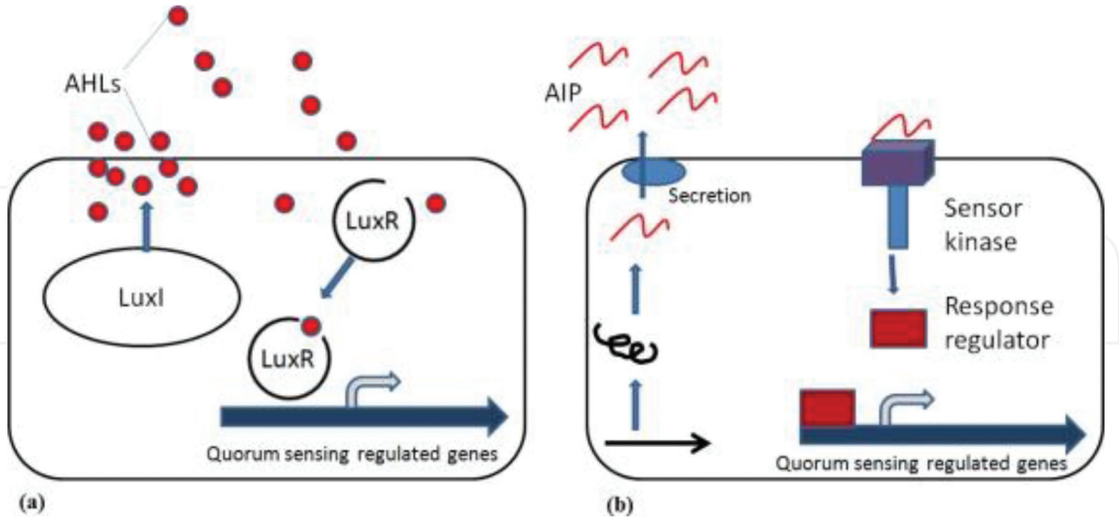

Figure 2. Schematic presentations of bacterial quorum sensing systems. (a) In Gram-negative bacteria, AHLs (filled circles) are produced by the LuxI synthase and will bind to the cognate LuxR receptor. The AHL-LuxR protein complex will bind to promoter DNA elements and regulate transcription of QS-regulated genes. (b) Gram-positive bacteria synthesize AIP (curvy lines) that are post-translationally modified and secreted. AIP detection occurs via a two-component signal transduction circuit, leading to the ATP-driven phosphorylation of a response regulator protein, which then binds to promoter DNA and regulates transcription of QS-regulated genes [34].

The periodontal microbiota is mostly heterogeneous and over 400 species have been defined in this habitat alone using a 16S rRNA amplification, cloning and Sanger sequencing approach [38].

Normally, the periodontal tissues remain healthy owing mainly to the numerous host protection mechanisms that work in the oral cavity [39].

Conceivably, the utmost unique and major host protection mechanism in the periodontium is the continuous passage of neutrophils from the underlying highly vascular periodontal tissue, through the connective and epithelial cell layers and into the gingival crevice. It has been estimated that approximately 30,000 polymorphonuclear neutrophils (PMNs) travel through periodontal tissue every minute and by this mean a constant contact between host neutrophils and the dental plaque biofilm will be facilitated [40].

The junctional epithelium surrounds the tooth surface and forms the "junction" between the tooth and host tissue. It is highly porous with large intracellular spaces and it contains no tight junctions and a lower number of desmosomes than the adjacent oral or sulcular epithelium [41].

Likewise, clinically healthy junctional epithelial tissue expresses high levels of IL-8, a potent neutrophil chemoattractant, that draws neutrophils to the adjacent dental plaque biofilm inhibiting biofilm growth (**Figure 3**) [42]. Additional host defense mediators associated with neutrophil exit from the vasculature and transit through the connective tissue, such as ICAM-1 and E-selectin, are also expressed in the appropriate tissues in clinically healthy periodontal tissue [43].

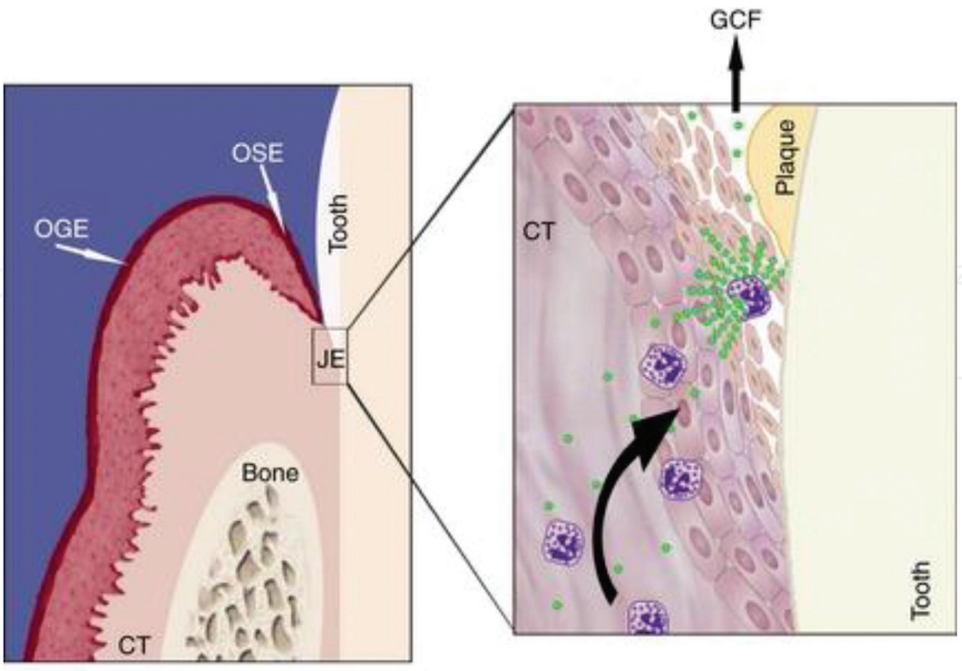

Figure 3. The junctional epithelium exemplifies a polymorphonuclear neutrophil degranulating upon bacterial stimulation [42].

More additional immunohistochemical and in situ studies have discovered that clinically healthy periodontal tissue also expresses human β defensin molecules 1, 2, and 3 along with soluble and membrane bound CD14 and lipopolysaccharide binding protein [44–46].

These innate defense proteins function in either bacterial killing or bacterial elimination, in line with the concept that healthy periodontal tissue is armed by the innate host defense system to protect against bacterial infection.

A study conducted by Beklen et al. defined the expression of TLR's 1–10 in both clinically healthy and diseased tissues [47].

Also the expression of antimicrobial peptides in response to microbial challenge as a result of the synergistic action of NOD1 and NOD2 with select TLRs has been described by Uehara and Takada [48].

Healthy periodontal tissue has been accompanying with a very simple supragingival plaque composition: few [1–20] layers of predominantly Gram-positive cocci (Streptococcus spp.: *S. mutans, S. mitis, S. sanguis, S. oralis*; *Rothia dentocariosa*; *Staphylococcus epidermidis*), followed by some Gram-positive rods and filaments (*Actinomyces* spp.: *Actinomyces viscosus*, *Actinomyces gerencseriae*, *Corynebacterium* spp.) and very few Gram-negative cocci (*Veillonella parvula*; *Neisseria* spp.). These latter are aerobic or facultative aerobic bacteria, capable to adhere to the non-exfoliating hard surfaces; initial adhesion is endorsed by surface free energy, roughness and hydrophilia, and is mediated by long- and short-range forces [49, 50].

4.4. Dental plaque mediated periodontal disease

Recent data from a number of laboratories propose that different types of periodontal disease may possibly have specific microbial etiologies.

Striking differences in microbial composition have been revealed upon examination of the microbiota in healthy and diseased periodontal tissues [51].

There have been two main hypotheses that explain the role of plaque bacteria in the etiology of periodontal diseases. The "Specific Plaque Hypothesis" proposed that, out of the diverse collection of organisms comprising the resident plaque microflora, only a few species are actively involved in disease [52].

This suggestion focused on controlling disease by targeting preventive measures and treatment against a limited number of organisms. In contrast, the "Non-Specific Plaque Hypothesis" considered that disease is the outcome of the overall activity of the total plaque microflora [53].

More recently, an alternative hypothesis has been proposed the "Ecological Plaque Hypothesis "that reconciles the key elements of the earlier two hypotheses. Significant features of this hypothesis are that, the selection of" pathogenic" bacteria is directly coupled to changes in the environment in addition diseases need not have a specific etiology; any species with relevant traits can contribute to the disease process [54].

A vital element of the ecological plaque hypothesis is that the disease can be prevented by direct targeting of the putative periodontal pathogens together with modifying the environment that is responsible for their enrichment [23].

5. The bacterial composition of biofilm in relation to periodontal disease

Microbiological analyses revealed that the composition of commensal oral bacteria and the bacterial load isolated from healthy sites are considerably different from that found in diseased sites.

Characterization of the periopathogenic microbial flora has shown that the microbial load is higher in periodontal pocket than in normal sulcus, also there is an increase in the number of Gram-negative organisms (15–50%) when compared to clinically healthy sites [55].

In the mid-1960s, Le et al. demonstrated the positive association between dental plaque and gingivitis [56].

Socransky modified Koch's postulates and, through associative and eliminative studies, identified a group of Gram-negative anaerobic bacteria able to induce periodontal deterioration [57].

He also classified several complexes of bacteria dividing them into groups, labeled by colors. The categories were based upon the pathogenicity of the bacteria and their role in inflammation and periodontal destruction (**Figure 4**) [58].

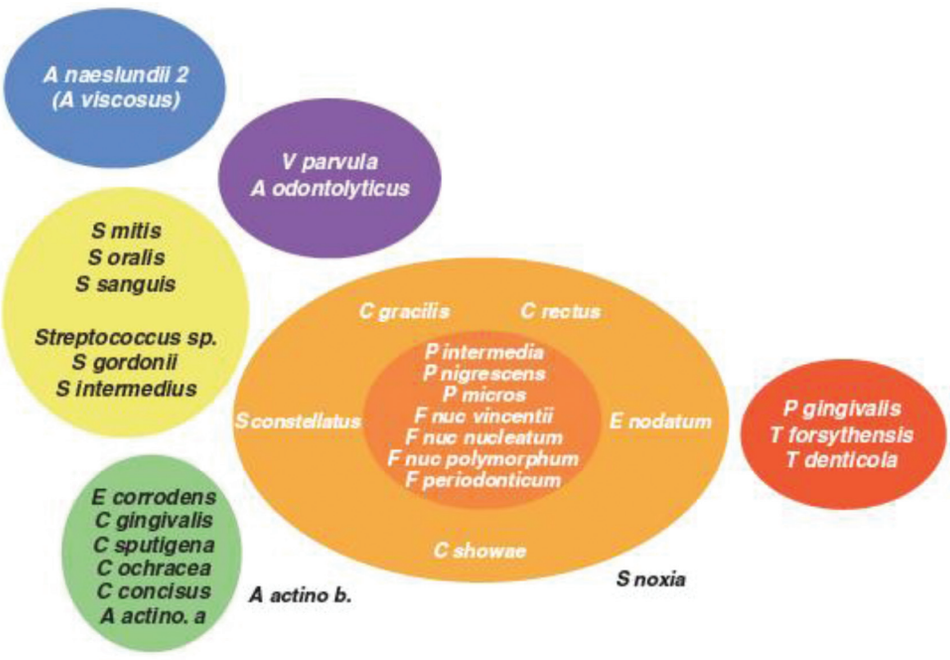

Figure 4. Microbial complexes in subgingival biofilm.

Early cultural analyses and current culture-independent molecular analyses of the periodontal microbiota have revealed profound ecological shifts in community structure associated with the transition from health to disease [59].

Recent advances based on independent metagenomic and mechanistic approaches propose that the pathogenesis of periodontal disease involves polymicrobial synergy and dysbiosis [60].

The dysbiosis of the periodontal microbiota indicates a change in the relative abundance of individual components of the bacterial community compared to their abundance in health, leading to alterations in the host-microbe crosstalk sufficient to mediate destructive inflammation and bone loss [61].

There is epidemiological evidence that plaque-induced gingivitis is the most prevalent periodontal disease and is more severe in individuals with poor oral hygiene [62].

Clinical gingivitis is associated with the development of a more organized dental plaque. Such biofilms are characterized by several cell layers (100–300), with bacteria stratification arranged by metabolism; besides the Gram-positive cocci, rods and filaments associated with healthy gingivae, the number of Gram-negative cocci, rods and filaments increases and anaerobic bacteria appear (*Fusobacterium nucleatum*, *Centruroides gracilis*, *Tannerella forsythia, Capnocytophaga* spp.) [63, 64].

The species involved vary depending on local environmental characteristics, but the colonization pattern is always the same [65].

5.1. Bacterial biofilm and the development of periodontitis

Periodontitis is a chronic inflammatory disease affecting tooth-supporting structures including the alveolar bone, connective tissue attachment, and gingiva [66].

The transition from gingivitis to periodontitis does not come about automatically, either in every patient or every site, but determined by three main factors: host susceptibility, pathogenic bacteria and "protective bacteria" [14].

Pathogenic bacteria possess virulence features that decrease the effectiveness of the host response by causing tissue breakdown and hindering tissue healing. Pili, fimbriae and blebs allow adhesion and colonization, and host defenses are impaired through a number of mechanisms: proteases that inhibit polymorphonuclear leukocyte (PMN) chemotaxis; capsules that mask LPS or increase resistance to phagocytosis; inhibition of PMN superoxide production.

The biofilm associated to periodontitis is complex and formed by many cell layers. The composition of the bacterial population in the active, destructive phase differs slightly from that during the remission period, adding support to the theory of the high specificity of pathogenic plaque; a preponderance of *Tannerella forsythia, P.gingivalis, T. denticola, C.rectus, P.intermedia* is associated with increasing probing depth and bleeding on probing (BOP) [58, 67, 68].

Based on classification system of periodontal disease and condition, two major forms of periodontitis are found, chronic periodontitis (CP) and aggressive periodontitis (AgP), which differ in clinical presentation, rate of progression, and, perhaps, age of onset [69].

5.2. The bacterial composition of biofilm in chronic periodontitis

Chronic periodontitis is an oral infection that results in destruction involving the gums, cementum, periodontium and alveolar process bone. The primary etiological factor of chronic periodontitis is bacterial plaque [70].

Chronic periodontitis is associated with heterogenic subgingival flora; however, the bacteria most cultivated in higher levels *are P. gingivalis, T. forsythia, P. intermedia, C. rectus, Eikenella corrodens, F. nucleatum, A. actinomycetemcomitans, P. micros, T. denticola, and Eubacterium* spp. Gram-negative anaerobes and capnophiles are dominant; spirochetes may also be present. In the sequence of initiation and progression of the inflammatory process, the subgingival bacteria increase in numbers and invade the pocket epithelial cells and, consequently, the underlying tissues. It has been proven that *A. actinomycetemcomitans* and *P. gingivalis* can invade the gingival tissues and this fact is distinctive for the more severe chronic periodontitis and aggressive periodontitis. Some recent data reveal that some herpes viruses present in the periodontal pockets, for example, Epstein-Barr virus-1 (EBV-1) and human cytomegalovirus (HCMV) [28].

5.3. The bacterial composition of biofilm in aggressive periodontitis

Aggressive periodontitis (AgP) is a form of periodontitis described by rapid and severe periodontal destruction in otherwise young healthy individuals. The etiology of periodontitis is very complex including the dental biofilm, which triggers the immuno-inflammatory response in a susceptible host [71].

The predominant microbiota in aggressive periodontitis is Gram-negative capnophiles and anaerobic rods. In localized aggressive periodontitis, *A. actinomycetemcomitans* is frequently present; this microorganism may comprise up to 90% of the cultivable microflora but essential levels of other microorganisms (*Capnocytophaga, E. corrodens, P. gingivalis*) have been found in periodontal pockets. In generalized form of aggressive periodontitis, *A. actinomycetemcomitans*, *P. gingivalis, P. intermedia, C. rectus* are prevailing. Herpesviruses, including Epstein-Barr virus-1 (EBV-1) and human cytomegalovirus (HCMV), can also be come across [28].

6. Systemic consequences of oral dysbiosis

Dysbiosis in periodontal disease as a trigger of bacteremia likely facilitates systemic dissemination of oral bacteria, and therefore good oral hygiene is crucial for controlling the total bacterial load. The link between oral pathogens and systemic effects has been evidenced by a recent study in animals, which found a direct effect of oral administration of *P. gingivalis* on the composition of the gut microbiome as well as inflammatory changes in various tissues and organs. Oral bacteria have been proposed to play a role in a number of systemic diseases, including cardiovascular disease, rheumatoid arthritis, adverse pregnancy outcomes, stroke, inflammatory bowel disease and colorectal cancer, respiratory tract infection, meningitis or brain abscesses, lung, liver or splenic abscesses, appendicitis, pneumonia and diabetes [72, 73].

7. Controlling oral communities

Oral biofilms play a major role in the etiology of oral diseases and have wide effects on quality of life and systemic health.

Many hypotheses were developed describing the ways by which dental plaque can exert its pathogenic potential. These hypotheses have been changed over time.

New understandings of the structure and composition of oral microbial communities have implicated shifts in the composition of the resident microbiota in the development of periodontal diseases and in that way the entire microbial communities could be considered as pathogenic [74].

Self-performed and professionally administered plaque controls are the mainstay in prevention of periodontal diseases.

Scaling and root planning together with self-performed plaque control have been shown to reverse the microbial shifts associated with periodontal diseases and reform subgingival microbiota similar to those found in periodontal health.

In addition to conventional approaches used to control oral biofilms, adjunctive treatments for periodontal diseases include systemically administered antibiotics, antiseptics and host-modulating agents have been developed with improvement in the clinical outcome of periodontal therapy [74].

As progress in the field of oral communities has increased, a new inhibitor or antagonist for dental plaque biofilm has been developed [75].

These are aimed to manipulate the structure or function of communities, endorsing health as opposed to disease. Some of these new methodologies target bacterial adhesion to host tissues, some target co-adhesion or co-aggregation and others struggle to harvest the natural armaments of commensal bacteria to affect the retention of others.

These successes in controlling the growth of specific periodontal pathogens in dental plaque pave the way for the development of strategies for manipulating more complex communities that are not so accessible (e.g., periodontal microflora) and that are more closely integrated with host tissues and host-cell functions [76].

Recently, transcriptional profiling of gingival epithelial cells stimulated with oral pathogens, for example P. gingivalis or A. actinomycetemcomitans, has revealed that specific responses for species predominate and that the core transcriptional response to oral organisms is limited [77].

The signal transduction within oral epithelial cells is designed to combat the challenging organism. Therefore, it might be possible to modulate host-cell signaling path ways to maintain a situation compatible with a healthy periodontal community [76].

8. Chapter summary

Oral microbial habitat is composed of wide variety of species. These species play a significant role in maintaining the health of the oral cavity by contributing in various ways. Resident microorganisms have coevolved and coexisted in a mostly harmonious symbiotic relationship.

The oral microflora can act as opportunistic pathogens when the habitat is altered or when microorganisms are found at sites not normally reachable to them.

In dysbiosis, the balance of the oral ecosystem is disrupted, allowing disease-promoting bacteria to manifest and cause conditions such as gingivitis and periodontitis.

Analysis of the microbiota reside in the oral cavity may be a useful approach to diagnose systemic diseases that have periodontal manifestations. The control of the total oral microbial load is important to prevent dissemination to other body sites.

Methods for the control of oral biofilms that are less dependent upon compliance and regular access to professional dental care are needed.

Approaches that intended to inhibit the attachment of oral microorganisms on oral surfaces or create long-lasting shifts in the oral microbiota hold much promise.

Future research exploring these and other possibilities will provide guidance on how to better prevent and manage periodontal diseases.

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